

Ordering Guidance for Genetic Testing for Familial Hypercholesterolemia

Familial hypercholesterolemia (FH) is an inherited disorder of lipid metabolism that results in elevated levels of low-density lipoprotein (LDL) cholesterol, and risk of heart disease at an early age. FH affects 1 in 250-300 Canadians; however, most are undiagnosed. Early identification of FH supports the use of medication to normalize life expectancy and genetic testing of at-risk relatives. Please see [Familial Hypercholesterolemia Implementation Recommendations](#) for additional details.

Individuals meeting one or more of the following criteria should be offered FH genetic testing:

- 1. Family history of confirmed FH:** Disease-causing pathogenic/likely pathogenic variant (mutation) in a close (1st or 2nd degree) blood relative (e.g. sibling, child, parent, parents' sibling, grandparent)
- 2. Extremely high LDL:** Personal history of high LDL cholesterol level of ≥ 8.5 mmol/L at any age
- 3. High LDL with additional features:** Personal history of untreated elevated LDL cholesterol level (not due to secondary causes). If baseline/untreated LDL cholesterol is unknown, an imputed level can be derived using the [CardioRiskCalculator](#):
 - Untreated LDL cholesterol level ≥ 5.0 mmol/L for age 40 years and over
 - Untreated LDL cholesterol level ≥ 4.5 mmol/L for age between 18 years and 39 years
 - Untreated LDL cholesterol level ≥ 3.5 mmol/L for age under 18 years**AND at least one of the following:**
 - Tendon xanthomas and/or corneal arcus in the patient
 - First-degree relative with high LDL cholesterol level (not due to secondary causes)
 - Proband or first-degree relative with early onset atherosclerotic cardiovascular disease (men under 55 years; women under 65 years)
 - Limited family history information (e.g., adopted)
- 4. Clinical judgement:** A clinician may use clinical judgement to order genetic testing in individuals who do not fit the above if advised by genetics and/or lipid disorder expert(s).

Additional considerations for the eligibility criteria above:

- Genetic testing in the pediatric population can be offered at any age, ideally in the first decade of life, guided by family history and/or lipid screening results.
- Prenatal diagnosis for FH does not change medical management.
- Routine results are expected in 6 to 8 weeks; expedited testing is not required.

How do I order FH genetic testing for my patient?

Please complete an FH genetic testing requisition from one of the testing labs: [Hamilton Regional Laboratory Medicine Program](#), [London Health Sciences Centre](#), and [Trillium Health Partners – Credit Valley Site](#). Your patient can take the requisition to a local community laboratory for bloodwork.

What should I do with abnormal or uncertain results?

For guidelines on management of FH, please see the [Canadian Cardiovascular Society position statement](#). Certain results (e.g., findings beyond your comfort level, variant of uncertain significance (VUS)) may require consultation with genetics and/or genetic counselling for your patient. Please consider the following options as needed:

- Visit [OTNhub](#) to connect with a genetics specialist through OTN eConsult
- Visit [Ontario Health](#) to find your local genetics clinic.